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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/028,989	12/28/2001	Ronald J. Pettis	7767-177409	4392

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EXAMINER	
BOUCHELLE, LAURA A	

ART UNIT	PAPER NUMBER
3763	

MAIL DATE	DELIVERY MODE
11/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/028,989	PETTIS ET AL.	
	Examiner	Art Unit	
	LAURA A. BOUCHELLE	3763	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *69-75,77-95 and 97-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *69-75,77-95 and 97-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/28/08,8/8/08,8/8/07,6/7/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

Applicant's arguments, see response and affidavit, filed 6/7/07, with respect to the arguments for the criticality of the exposed height of the needle outlet have been fully considered and are persuasive. The previous rejections of the claims have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of Gross (USPN 5,527,288) in view of Prausnitz (USPN 6,611,707) in further view of Srivastava (USPN 6,007,821). See below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 69-75, 77-89, 93-95 and 97-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gross (US Pat# 5,527,288) in view of Prausnitz (USPN 6,611,707) in further view of Srivastava (USPN 6,007,821). Gross discloses an intradermal compartment drug delivery device that includes administering a substance through a small gauge hollow needle. The length of the needle is between 0.3 to 3.0 mm. Gross discloses that "the drug is delivered directly to a capillary-containing tissue and has no barriers to pass through before entering the vascular system". See 3:50-52. This capillary-containing tissue is the intradermal compartment even though that term is not used in Gross' specification. The diameter of the needle is 0.1-

0.2mm. The substances for injection include a variety of substances that include peptides, proteins, hormones, insulin, nucleic acids, and hydrophobic and hydrophilic compositions. See 6:59+. As shown in figure 3, the needle is inserted perpendicularly into the skin. Means for actively discharging the drug include an infusion pump. See 2:31-35. The disclosure also indicates that the device can be used to deliver a bolus injection (applicant's disclosure defines a bolus as an amount delivered in less than 10 minutes, see Summary paragraph 22). See 3:29-32. Example 1 and 2 disclose an infusion flow rate of 0.1 ml/min. See 10:60+.

Gross meets the claim limitations as described above but fails to include that the needle has an outlet with an exposed height of between 0mm-1mm. However, Prausnitz teaches the use of needles with a zero exposed height to deliver drugs into the skin. See 3:27-28.

At the time of the invention, it would have been obvious to use the teaching of the exposed outlet of Prausnitz in the invention of Gross in order to provide a known flow dynamic as desired from the end of the needle. The zero exposed height as disclosed by Prausnitz would be known by one skilled in the art to provide a substantially longitudinally directed flow as opposed to a radially directed flow component as found in beveled needles with liquid exits the needle opening.

Gross meets the claim limitations as described above but fails to include that the dosage of the substance for achieving a systemic bioavailability is reduced by at least 10%-30% compared to when the substance is delivered to a subcutaneous compartment. However, Srivastava discloses a method for treatment of autoimmune disease that includes the teaching that "while both subcutaneous and intradermal routes of administration are effective, intradermal injections typically require a lower dosage and are, therefore, preferred with respect to economy

of materials". See 20:3-6. As demonstrated in the example in section 6 the effective dose is 100 μg subcutaneously and 10 μg intradermally, i.e. 10% less. See 20:7-10. Additionally, if one understands bioavailability to be the amount of a given dosage that reaches the blood compartment or plasma concentration of the drug, then one would reasonably conclude that the effective dose could only be reduced for intradermal administration in the above example if systemic bioavailability was being reached. Furthermore, one can reduce (as taught by Srivastava) the dosage of the substance by at least 30% or more to achieve systemic bioavailability to some degree.

At the time of the invention, it would have been obvious to use the invention of Gross to administer the composition at the reduced intradermal dosage value (from 10 to 30 percent) as taught by Srivastava. Both devices are analogous in the art of intradermal drug delivery; therefore, a combination is proper. Additionally, Srivastava teaches that intradermal injection is a preferred route of delivery for the gp96 protein and Gross teaches that typical drugs for delivery include proteins. One skilled in the art would recognize that the motivation for the combination would be to use the device of Gross for its intended use. Furthermore, the motivation for the combination can be found in common knowledge in the art. Intradermal injection systems, such as the device by Gross, are well known in the art for delivering a wide array of substances into the intradermal compartment. One skilled in the art would reasonably make the combination in light of common knowledge that devices such as Gross' exit for delivery into the intradermal compartment and the method of Srivastava would be optimally performed by using the device by Gross.

Claims 69-75, 77-89, 90-95 and 97-107 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Lee et al (USPN 5,250,023) in view of Srivastava.

Lee discloses an intradermal compartment drug delivery device that includes administering a substance through a small gauge hollow needle array of at least 6 needles (4 and 14). The length of the needle is between 0.3 to 2.0 mm. The substances for injection include a variety of substances that include peptides and proteins. As shown in figures 1-2, the needle is inserted perpendicularly into the skin. Regarding the exposed height of the needle outlet, it is inherent that the needle has at least an exposed height of at least 0mm. An exposed height of at least 0mm is required and necessary since the device teaches delivery of a substance through the needle and therefore requires that the needle have at least a non-beveled opening that results in an exposed height of 0mm.

Lee meets the claim limitations but fails to include that the dosage of the substance for achieving a systemic bioavailability is reduced by at least 10%-30% compared to when the substance is delivered to a subcutaneous compartment. However, Srivastava discloses a method for treatment of autoimmune disease that includes the teaching that "while both subcutaneous and intradermal routes of administration are effective, intradermal injections typically require a lower dosage and are, therefore, preferred with respect to economy of materials". See 20:3-6. As demonstrated in the example in section 6 the effective dose is 100 μg subcutaneously and 10 μg intradermally, i.e. 10% less. See 20:7-10. Additionally, if one understands bioavailability to be the amount of a given dosage that reaches the blood compartment or plasma concentration of the drug, then one would reasonably conclude that the effective dose could only be reduced for intradermal administration in the above example if systemic bioavailability was being reached.

Furthermore, one can reduce (as taught by Srivastava) the dosage of the substance by at least 30% or more to achieve systemic bioavailability to some degree.

At the time of the invention, it would have been obvious to use the invention of Lee to administer the composition at the reduced intradermal dosage value (from 10 to 30 percent) as taught by Srivastava. Both devices are analogous in the art of intradermal drug delivery; therefore, a combination is proper. Additionally, Srivastava teaches that intradermal injection is a preferred route of delivery for the gp96 protein and Lee teaches that typical drugs for delivery include proteins. One skilled in the art would recognize that the motivation for the combination would be to use the device of Lee for its intended use. Furthermore, the motivation for the combination can be found in common knowledge in the art. Intradermal injection systems, such as the device by Lee, are well known in the art for delivering a wide array of substances into the intradermal compartment. One skilled in the art would reasonably make the combination in light of common knowledge that devices such as Lee's exit for delivery into the intradermal compartment and the method of Srivastava would be optimally performed by using the device by Lee.

Response to Arguments

Applicant's arguments filed 7/25/05 were in response to a previous rejection using some of the references above. The response below pertains to the previous rejection(s) that are maintained above. The arguments filed 7/25/05 have been fully considered but they are not persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the knowledge generally available to one of ordinary skill in the art would reasonably lead one to the combination above. The knowledge is founded on the fact that intradermal delivery devices such as the device of Gross are well known in the art and are purposely designed to carry out methods such as the one taught by Srivastava.

In response to applicant's argument that there is no reasonable expectation of success, the examiner recognizes that the Srivastava reference does not state the claim language or the outcome of the method verbatim. However, the claimed method is very broad. Specifically, the claim limitation that states "wherein the dosage of the substance for achieving a systemic bioavailability of the substance is reduced..." can be broadly interpreted. Applicant provides no quantative or relative measure for the term bioavailability. Therefore, as long as one achieves at least some bioavailability, regardless of the amount in reduction of the dose, one would read on the claim language. Even if a reduction in the dosage given via intradermal administration resulted in reduced systemic bioavailability, albeit at least some of the substance reaching the blood compartment or plasma, that reduced systemic bioavailability would still read on "for achieving systemic bioavailability" since no quantative or relative measure is claimed for the bioavailability. Hence, there is a reasonable expectation of success with the combination of

references above since the method of Srivastava clearly teaches reducing the dosage for treating autoimmune disease which necessitates at least some of the substance being delivered to the blood compartment or blood plasma, i.e. bioavailability.

In response to applicant's arguments that the prior art does not teach the exposed height of the opening of the needle, see the new rejection above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA A. BOUCHELLE whose telephone number is (571)272-2125. The examiner can normally be reached on Monday-Friday 8-4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nicholas Lucchesi can be reached on 517-272-4977. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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